

Beyond the Elimination Diet: Reintroduction of Foods in IgE- and Non-IgE Mediated Food Allergies

Wendy Elverson, RD, CSP, LDN
Senior Clinical Nutritionist
Center for Nutrition
Boston Children's Hospital
Wendy.Elverson@childrens.harvard.edu
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Disclosures

- Honorarium provided by Nutricia
- Consultant positions
 - Nutricia advisory board meeting
 - Nutricia cow milk allergy/multiple food allergies dietary management flow chart

None pose any conflict of interest for this presentation

The opinions reflected in this presentation are those of the speaker and independent of Nutricia North America

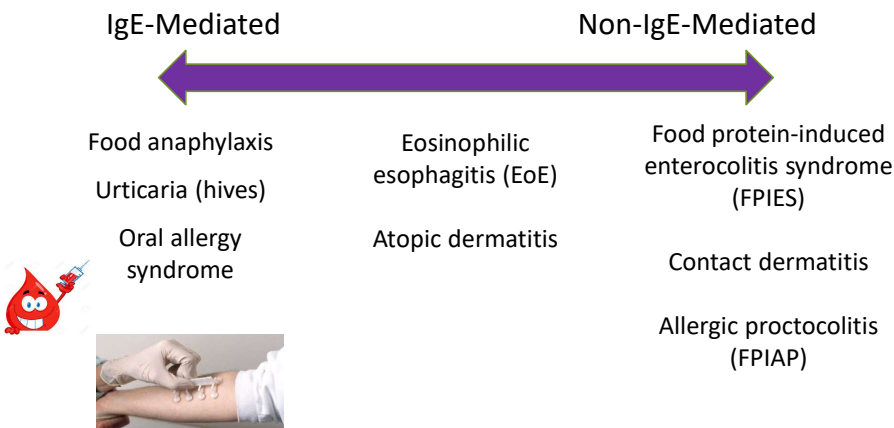
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Objectives

- Explain the dietitian's role following physician-ordered introduction and reintroduction of allergens with cow milk allergy, egg allergy, food protein-induced enterocolitis syndrome (FPIES), and eosinophilic esophagitis (EoE)
- Illustrate support for the caregiver of children with food allergic conditions during the time of food reintroduction
- Apply information on food re-introduction to real world scenarios

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Spectrum of Food Allergies



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Let's meet Jane

Jane is a 6 mo. born at 38 weeks, no complications. Lives with parents, first baby. Mother has a h/o of anxiety. Planning to return to work, in-person FT, when Jane is 9 months. Father working FT. Extended family out of state.

8 weeks, persistent mucus and visible blood in her stools, some irritability. Stools guaiac positive X2 at pediatrician. Mother eliminated all dairy from her diet → Jane's symptoms resolve within 2 weeks. Mother remains on cow's milk-free diet.

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Let's meet Jane

Exclusively breastfeeding → at 4 months introduced one at a time to **avocado, banana, carrots and butternut squash**

5 mos. of age, 3rd exposure to infant **oatmeal** mixed with pear → 2 hours later she proceeded to have vomiting, 6X in 1 hour → presented to ER lethargic with altered mental status (minimally responsive, decreased tone, tachycardia) → IV placement unsuccessful.

Tx to Children's Hospital → IVF and Zofran. Developed diarrhea with mucus, heme-positive stool. D/c after 36 hours, nursing well, continued diarrhea with mucus and microscopic blood in stool.

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Jane's Presumed Diagnosis

FPIES to oat and ? pear

Food protein-induced allergic proctocolitis (FPIAP)

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Parental Concerns

- ❑ Fearful of reintroducing solid foods.
- ❑ Mother avoiding in her diet cow's milk, soy, pear, egg and all grains. Should she continue?
- ❑ Etiology of diarrhea, which has improved?
- ❑ Father shared mother often tearful.
- ❑ Both parents shared mother's anxiety about plan to return to work in about 3 months



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What would you recommend?

RD visit, 2 weeks after discharge. Stools normalizing and guaiac negative. Mother on a pear, grain, cow’s milk and soy free diet.

- A. No solids until Jane is 8 months of age. Continue breast milk (BM). Mother’s diet: No cow’s milk, soy, pear, oat. Offer option of supplemental hypoallergenic (HA) formula
- B. Introduce rice cereal as a source of iron. Next introduce a few fruits and vegetables, then egg and peanut. Continue BM. Mother’s diet: No cow’s milk, no pear, no oat. Offer supplemental HA formula as an option
- C. Continue BM with option for supplemental HA formula. Introduce 1 new food at a time starting with single ingredient foods in low-risk category. Mother’s diet continue to avoid cow’s milk; add back pear, oat, rice and soy into maternal diet.
- D. Wean BM, start HA formula and introduce Jane to single ingredient foods in the low risk FPIES category

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FPIAP

FOOD PROTEIN-INDUCED ALLERGIC PROCTOCOLITIS

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Allergic Colitis/FPIAP: Overview

Data

- Very limited; Mostly case series or small observational studies
- Wide variations in practice patterns due to limited data, 0.16 to 64% incidence

Symptoms

- Rectal bleeding: visible and/or microscopic blood in stool, mucus in stool.
- In some cases associated with feeding difficulties and irritability

Onset (2 to 8 weeks of age)

Caubet et al. Non-IgE-Mediated Gastrointestinal Food Allergies in Children. *Pediatric Allergy and Immunology*. 2017 Feb;28(1):6-17.
Kaya et al. Characteristics and Prognosis of Allergic Proctocolitis in Infants. *JPGN*. 2015
Lake et. Al. Food Induced Eosinophilic Proctocolitis *JPGN* 2000.

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Allergic Colitis/FPIAP (Cont.)

Triggers

- **Cow's milk, egg, soy, corn** (and others)

Breastfed infant

- Maternal restriction of triggers

Formula-fed infant

- Majority tolerate an extensively hydrolyzed formula but 5-10% may need amino acid-based formula

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Allergic Colitis/FPIAP: Reintroduction

Timing: Most but not all tolerate presumed triggers by one year of age. Resolution: 7-12 months, can be longer.

Xanthakos et al. JPGN 2005 Jul;41(1):16-22.
Lazare et al. J Hum Lact. 2020 Feb;36(1):168-172.

Reintroduction: standard protocol does not exist. Shared decision making with caregiver(s) and providers

Ladders are common practice, particularly with non-IgE-mediated (**except** FPIES) cow’s milk allergy and egg, but needs more research and standardization

◦ *Venter, C, Meyer R., Motohiro, E et. Al. Food Allergen Ladders: A need for standardization. Pediatric Aller and Immunol. 2022 Jan;33(1):e13714.*

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Patient Specific Factors for Favorable Use of Food Ladders: *Venter et al. Pediatr Allergy Immunol. 2022;33:e13714.*

Further study and standardization needed	Non-IgE-mediated (except FPIES)
	IgE-mediated with prior mild, non-anaphylactic reactions
	Non-asthmatic is ideal, with stable, treated asthmatics potentially suitable
	Willing and prepared patients/families without language or comprehension barriers
	Low or decreasing skin prick test wheal or serum specific-IgE levels
	Younger patients are preferable

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FPIES

FOOD PROTEIN-INDUCED ENTEROCOLITIS SYNDROME

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Acute FPIES: What are the Symptoms

Symptoms generally start 1-4 hours post ingestion

- Repetitive vomiting, generally profuse and severe
- Diarrhea may also occur (onset usually within 24 hours, can be bloody)
- Lethargy, pallor, dehydration
- Severe reactions: risk of shock, thrombocytopenia, methemoglobinemia
- Does not necessarily occur with first infant exposure to a new food

Unlike IgE-mediated food allergies symptoms such as hives, wheezing, itching and/or anaphylaxis do NOT occur with FPIES

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Acute FPIES

- Non-IgE-mediated disorder
- US prevalence study
 - Adults = 0.28%
 - Children < 18 yrs = 0.51%
 - Nowak-Wegrzyn A, et al JACI 2019
- USA: Cow's milk, soy, rice, oat
- Food triggers vary somewhat by geographical location
- Typically presents < 9 mos. of age
 - Cow's milk/soy: 1-3 mos.
 - Solid food: 4-7 mos.

Nowak-Wegrzyn, et al. J Allergy Clin Immunol. 2017;139:1111-26.e4.

Professional and Caregiver Resource: I-FPIES (International FPIES Association)

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Management of FPIES

Elimination of causative foods

Ensure advancement of solids (RD is key)!!

Management of reactions

- Severe reactions: emergency room: risk of shock
- IVF
- Ondansetron may be used/ steroids may be used
- Epinephrine not indicated

Skin and SIgE testing may be done to rule out atypical FPIES

Emergency room letter and other resources

Multidisciplinary support

Known triggers: Challenges should **NOT be done at home**. Challenges done under medical supervision with IV access in place. Generally, challenges not performed fewer than 18 months post last reaction.

Nowak-Wegrzyn, et al. J Allergy Clin Immunol. 2017;139:1111-26.e4.

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FPIES Food Triggers

Mt. Sinai 2013 (160) (children and adults)	CHOP 2014 (462)	Baylor/Texas Children's 2019 (74)	Multicenter 2020 (441)	Australia 2017 (230)
Cow's milk (44%)	Cow's milk (67%)	Rice (53%)	Cow's milk (53%)	Rice (45%)
Soy (41%)	Soy (41%)	Cow's milk (49%)	Soy (37%)	Cow's milk (33%)
Rice (22%)	Rice (19%)	Oats (35%)	Rice (34%)	Egg (12%)
Oat (16%)	Oat (16%)	Soy (31%)	Egg (23%)	Oat (9%)
Barley (4%)	Egg (11%)	Banana (24%)	Sweet potato (17%)	Chicken (8%)
Poultry (4%)	Wheat (10%)	Sweet potato (22%)	Wheat (16%)	Soy (5%)
Beef (4%)	Corn (8%)	Avocado (16%)	Avocado (13%)	Banana (4%)
Sweet potato (3%)	Chicken (4.5%)	Squash (12%)	Peanut, banana (12%)	Wheat, beef, pear, sweet potato (3%)
Egg (3%)	Turkey (4.1%)	Apple (11%)	Pea, fish, beef (9%)	Avocado, apple, pumpkin, white fish, tuna (2%)
Wheat, corn, green pea (< 0r =1%)	Sweet potato (4.1%)	Chicken, corn, carrot(7%)	Apple (8%)	Corn, lamb, carrot, peas (1%)
Fish/Shellfish (~9%)*	Banana (3.5%)	Wheat, green bean (5%)	Corn, chicken (7%)	
	Peas (3.2%)	Quinoa, white potato, pea (4%)	Squash, shellfish (6%)	
	Beef (2.4%)	Mango, nuts, turkey (3 %)	White potato (5%)	
	Peanut (1.9%)		Multiple foods (4% or less)	

J Allergy Clin Immunol Pract. 2013 Jul-Aug;1(4):343-9.; J Allergy Clin Immunol. 2014 Aug;134(2):382-9.; Pediatrics. 2003 Apr;111(4 Pt 1):829-35; Annals Allergy Asthma Immunol, 2019 April:407-11; J Aller Clin Immunol Pract. 2020;8:1702-9; J Allergy Clin Immunol. 2017*140(5); 1323-30

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Number of Food Triggers

CHOP 2014 (462)	Baylor/Texas Children's 2019 (74)	Multicenter 2020 (441)	Australia 2017 (230)
70% (1-2 foods)	31% (1 trigger)	31% (1 food group)	68% (1 food)
25% (3-6 foods)	18% (2 triggers)	17% (2 food groups)	20% (2 foods)
5% (≥ 7 foods)	51% (≥3 triggers)	17% (3 food groups)	7% (3 foods)
		12% (4 food groups)	6% (≥ 4 foods)

J Allergy Clin Immunol. 2014 Aug;134(2):382-9.
Pediatrics. 2003 Apr;111(4 Pt 1):829-35
Annals Allergy Asthma Immunol, 2019 April:407-11;
J Aller Clin Immunol Pract. 2020;8:1702-9; J Allergy Clin Immunol.
2017*140(5); 1323-30

Adapted from Nowak-Wegrzyn, et al. J Allergy Clin Immunol. 2017;139:1111-26.e4.

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Solid Food Introduction in Infants with FPIES

Food Group	Low Risk	Moderate Risk	Higher Risk	Highest Risk
Vegetables	Broccoli, cauliflower, parsnip, pumpkin	Carrot, squash, white potato, string bean	Sweet potato, green pea	
Fruits	Blueberry, peach, plum, prune, strawberry, watermelon	Apple, pear, orange	Banana, avocado*	
Proteins/Fats	Tree nut and seed butters# (almond butter, sunflower seed butter, tahini), canola oil, coconut oil	Beef, peanut butter ??*, legumes (other than pea and soy) olive oil	Chicken, turkey, eggs, fish, peanut butter??*	Cow’s milk, soy
Grains/Grain like foods	Millet, quinoa flakes (flakes can be made into hot cereal)	Corn, corn grits , wheat, cream of wheat, barley, white potato		Rice, oat

#Nut butters thinned with water or mixed in purees
*Anecdotaly, seeing more avocado and peanut reactions in clinical practice

Adapted from Nowak-Węgrzyn, et al. J Allergy Clin Immunol. 2017;139:1111-26.e4.

Texture Advancement

Thin puréed → thicker puréed→ dissolvable solid → soft mashable

Food	Thin	Thick	Dissolvable	Soft Mashable
Peach	Stage 1	Pureed fresh	Freeze dried	Canned, steamed, ripe pieces
Quinoa	Quinoa flakes thinned	Quinoa flakes	Puffed quinoa	Homemade pancake
Beef	Stage 1	Home pureed	----	Ground, finger shaped
Broccoli	Pureed and thinned	Pureed	----	Overcooked pieces
Corn	Grits thinned	Grits	Corn puffs cereal, puffed corn snacks	Homemade pancake, corn fork mashed

Caregiver Creativity



Millet porridge

- Ingredients:
 - Water
 - Ragi or millet flour
- Directions:
 - Mix 1 tablespoon of the ragi powder with 6 tablespoons of water in a small frying pan
 - Place on the stove and mix consistently until there’s a slight boil to the water. Turn the gas burner off while still mixing.
 - Mixture should come out somewhat like a paste when it’s done (only takes 2-3 minutes total on gas stovetop).

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Jane

Fruits

Vegetables

Proteins

Grains

Calcium

Fats

Shared Decision Making

5 to 7 months

7 to 9 months

9-12 months

- Initially started off slow: 1 new food every 7 to 10 days. Offer 1-2 times per day. Started with 1/8 tsp and double each dose
- Pumpkin, cauliflower, peach, broccoli, parsnip, beef

Consultation with psychologist in allergy program

- Lower risk foods 1 every 3 days, start with 1 TBSP; Moderate risk, one every 5 days start with ¼ tsp. Introduce supplemental hypoallergenic (HA) formula
- Pumpkin, cauliflower, peach, broccoli, parsnip, beef, blueberry, carrots, quinoa

Rx: 400 IU of vit. D

- Mother back at work and baby in day care. Drinking breast milk and HA formula. Continues food introductions
- Pumpkin, cauliflower, peach, broccoli, parsnip, beef, blueberry, prune/plum, carrots, spinach, quinoa, white potato, corn, strawberries, apple, coconut oil, corn oil, peanut, almond

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Jane: 12-24 months



- Growing and eating well
- Baked cow's milk introduced → yogurt → transitioned to whole milk
- Baked egg introduced and then omelet strips
- Consuming a variety of foods including wheat, rice, soy, tree nut butters, chicken, turkey, peas, sweet potato
- Continues to avoid oat and pear

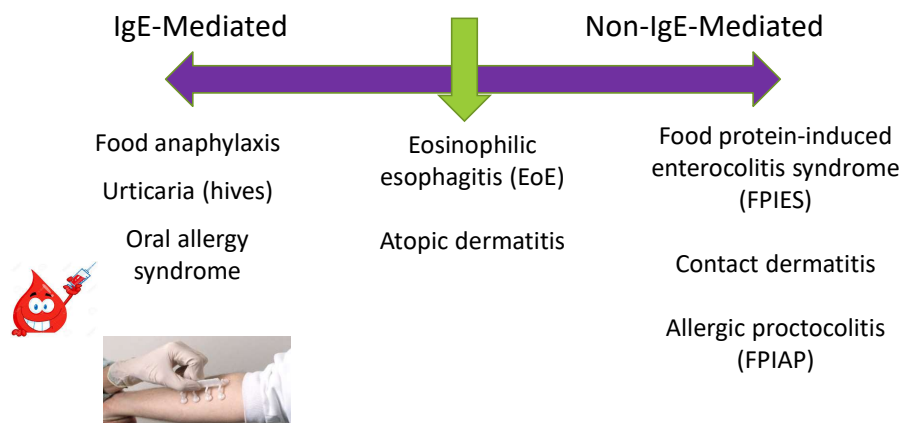
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EoE

EOSINOPHILIC ESOPHAGITIS

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Spectrum of Food Allergies



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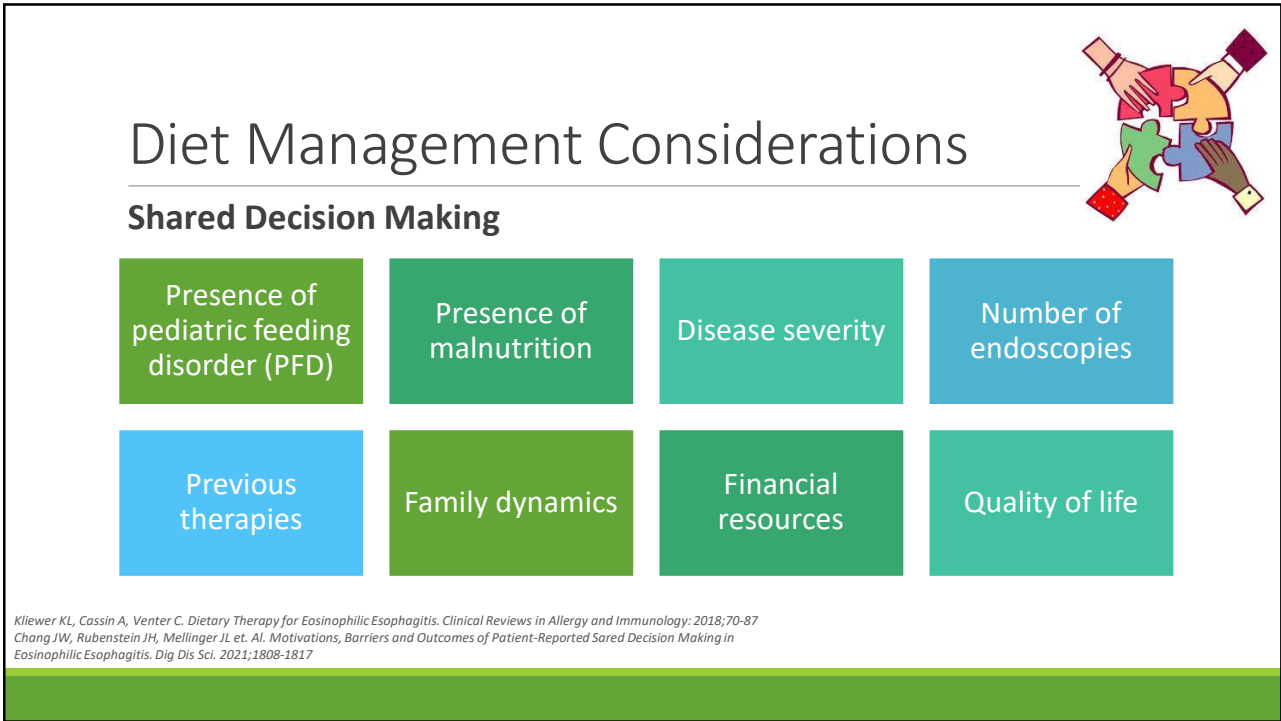
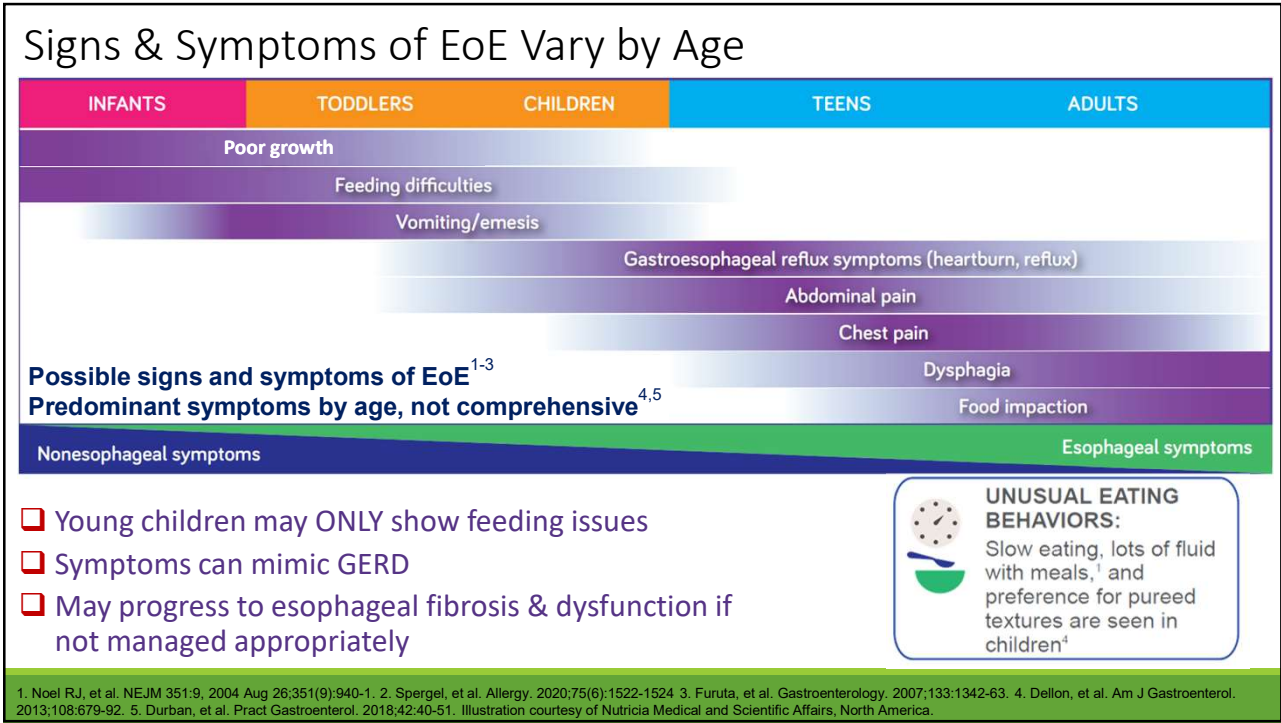
EoE Management Options

Immune response to food antigens resulting in infiltration of eosinophils in the esophagus

Management:

- Diet
 - Elemental diet (amino acid-based formula)
 - Empiric elimination diet
 - Targeted elimination diet
- Medical:
 - Proton pump inhibitor (PPI)
 - Topical swallowed steroids
 - Biologics
 - Dilation

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Elimination Diet Approaches for EoE

Dietary approach	Elimination diet details	Remission rate
Elemental	Amino acid-based formula +/- a few fruits and vegetables	74-100%
Empiric	Eliminate likely trigger foods	-
• 6FED/SFED	8 most common food allergens (cow’s milk, soy, egg, wheat, peanuts/tree nuts, fish/shellfish)	74-81%
• 4FED/FFED	Cow’s milk, wheat, soy, egg	64%
• 2FED/TFED	Cow’s milk, wheat	-
Allergy test-directed	Eliminate specific foods based on results of allergy testing	35-57%
Allergy test-directed	Eliminate specific foods based on results of allergy testing plus cow’s milk	77%

One food elimination diet (cow’s milk),
less data available (50-64%)

Kagalwala A, Dig Dis 2014;32:114-19
Cianferoni and Spergel J. Clinial Rev Allerg Immunol. 2016;50:159-74
Kliewer KL, Cassin AM and Venter C/ Clinic Rev Allerg Immunol. 2018;55:7-87
Lucendo AJ. Minerva Gastroenterology 2022;49:59

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Stepping Up or Stepping Down ?

- Step up approach (start with 1-2 food)
- Eliminate foods with each step
 - Molina-Infante et. Al. J Allergy Clin Immunol. 2017



Gold standard 8-week trials followed by EGD

RD
Detective

- Step down approach (start with SFED or FFED and add back foods)
- Add foods with each step



Kliewer KL, Cassin AM and Venter C/ Clinic Rev Allerg Immunol. 2018;55:7-87
Wechsler JB, Schwartz S et. Al. Clinical Gastroenterology and Hepatology March 2021
Lucendo AJ. Minerva Gatroenterol. 2022

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Baked Egg and Baked Milk in IgE-mediated Egg and Cow Milk Allergy

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Vignette

2 YO female with cow milk, peanut, egg allergies; passed baked milk and baked egg challenge

Phone call to nursing:

- 1) Ella is tired of the standard baked milk and baked egg muffin recipe what else can we bake?
- 2) Can Ella just eat store bought products with egg and/or cow's milk as 3rd ingredient or must we bake at home?
- 3) Can Ella now have pudding and chocolate mouse?
- 4) If the muffins are soggy in the middle, can we still use them?
- 5) What is the minimum amount of flour to be used for 1 cup milk or 2 eggs in 6 servings recipe? A: ½ cup; B: 1 cup; C: 1 ½ cups; D: 2 cups

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2) Can Ella just eat store bought products with egg and/or cow's milk as 3rd ingredient or must we bake at home?

No, unfortunately amount of egg and/or cow's milk in commercial products proprietary information

3) Can Ella now have pudding and chocolate mouse?

No, these items do not incorporate a flour matrix

4) If the muffins are soggy around the blueberries and raisins can we still use them?

No, use mashed fruit or sprinkle fruit or chocolate chips on top

5) What is the minimum amount of flour to be used for 1 cup milk or 2 eggs in 6 servings recipe?

B) 1 cup flour

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Creative Baked Milk and Baked Egg Ideas



Homemade:

- Muffins/cupcakes
- Breads, rolls
- Biscuits/crackers (milk)
- Pizza crust (milk)
- Oatmeal bake

Store bought/commercial, 3rd ingredient or further

- Crispy cookies
- Muffins
- Waffles/pancakes
- Breads, English muffins
- Pizza crust*
- Crackers/snacks*

*Do not add cheese.

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Conclusion

Introduction and reintroduction, when medically indicated, can improve quality of life and nutrient density

FPIAP and EoE triggers generally introduced at home

FPIES triggers always introduced under medical supervision

Shared decision making and motivational interviewing is important

Registered dietitian key to helping families with how to introduce and detecting unknown ingestions

Elimination diets: It takes a village